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PERFORMANCE DIFFERENCES BETWEEN TWO GROUPS OF COMMERCIAL
PIGS FOLLOWING EXPERIMENTAL INFECTION WITH PRRS VIRUS 1-7-4

BY

ERIN LITTLE

A thesis submitted in partial fulfillment of the requirements for the

Master of Science

Major in Animal Science

South Dakota State University

2019

THESIS ACCEPTANCE PAGE

Erin Little

This thesis is approved as a creditable and independent investigation by a candidate for the master's degree and is acceptable for meeting the thesis requirements for this degree.

Acceptance of this does not imply that the conclusions reached by the candidate are necessarily the conclusions of the major department.

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ACKNOWLEDGMENTS

I would like to sincerely thank **Dr. Michael Gonda** for all the direction and guidance over the last two years. I especially appreciate your flexibility and open-mindedness to take on a swine project. My work schedule prevented me from being at the university on a normal schedule but you have been available remotely and at all hours to offer advice and answer questions. For that, I genuinely appreciate your time!

To **Dr. Scott Dee**, I very much appreciate all of your support and guidance over the last four years at Pipestone. Not only have you taught me so much about applied research but you planted the grad school idea in my head and helped make it real. You've always treated me like another "scientist" and I thank you so much for that! You are a great mentor, teacher and friend. **Dr. Michael MacNeil**, I greatly appreciate your time and direction during this project. You have taught me to think critically and not be afraid to question the way it's 'always been done'.

PAR and Pipestone team, all of you have been very helpful while I have been completing this project. I wouldn't have been able to do it without the team stepping up to help with work projects during busy school days. Your willingness to help me continue my education while still continuing to work has been vital to my completion and I thank you all for that. To **Jenelle and the TN team**, I would like to thank you for allowing me to use a portion of your trial as my research project. Your support has been very valuable and I truly couldn't have conducted this project while working without TN's encouragement and guidance.

Family and friends, thank you all for your support. From the moment I decided to dive back into school everyone has been super helpful. **Mom, Dad, Ben, Pete and Deb**, you have all been in my corner even from hours away, I really appreciate it. **Andrew**, thanks for doing lots of pig chores for me on weekends and loading pigs at night so I could catch up on homework and writing - thanks brother!

Finally, my biggest thanks go to **Derek**. Remember when we decided to buy a farm, get married, work two full time jobs, and then I brought up the idea of going back to school, simultaneously? The entire time you have been fully supportive, I seriously couldn't have done it without you. You have really been the best husband/friend/therapist/roommate/chore-help that a girl could ask for.

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ABSTRACT

PERFORMANCE DIFFERENCES BETWEEN TWO GROUPS OF COMMERCIAL
PIGS FOLLOWING EXPERIMENTAL INFECTION WITH PRRS VIRUS 1-7-4

ERIN LITTLE

2019

Porcine reproductive and respiratory syndrome virus (PRRSV) is the costliest swine disease in North America. Vaccines and management alone have not been effective in controlling this disease. Genetic selection for resilience may be a complimentary approach for controlling PRRSV. The objective of this study was to estimate performance differences between two groups of pigs from the same commercial line following infection with PRRSV 1-7-4: 1) pigs sired by boars selected based on a standard index (TN-S), which emphasized feed efficiency and carcass quality; and 2) pigs sired by boars selected based on an experimental index (TN-E), which emphasized feed intake, piglet vitality, and robustness. Potential welfare and cost concerns of the use of PRRSV 174 to individually infect >1400 animals led to conduction of a pilot study to understand morbidity and mortality of PRRSV vaccinated and unvaccinated pigs. Results showed a 22% mortality in unvaccinated pigs and 5% in vaccinated pigs. Thus, use of PRRSV 174 would provide a robust challenge but vaccination reduces excessive cost and mortality. Pigs ($n \cong 730$ per sire group) were housed in a commercial research wean-to-finish barn. Experimental unit was pen, 27 pens per genetic group. All pigs were vaccinated for PRRSV with PRRS MLV at weaning. Four weeks after weaning, all pigs were experimentally infected with 2mL of 1-7-4 PRRSV at 3.5 logs of

TCID₅₀/mL. Average daily gain (ADG), average daily feed intake (ADFI), and carcass characteristics were measured. Statistical analyses were performed using a linear mixed model with sire group (TN-S or TN-E) as a fixed effect. The TN-E group had 0.06 kg/day greater ADFI than the TN-S group from 0 to 42 dpi ($P=0.01$). Feed conversion ratio (FCR) was 0.06 ($P<0.001$) and 0.12 ($P=0.03$) less for the TN-S group from weaning through finishing and for 0 to 42 dpi, respectively. Percent lean was 0.6% ($P=0.02$) greater for the TN-S group. Pigs sired by boars selected using the experimental index showed no significant difference in ADG, but had greater ADFI post-challenge, while pigs sired by boars selected based on the standard index had significantly lower FCR.

Chapter 1
LITERATURE REVIEW

Introduction

This review focuses on studies conducted during the postweaning period that assess genetic variation in the performance of pigs in production environments; with particular emphasis on their response to a challenge with porcine reproductive and respiratory syndrome virus (PRRSV). One goal of applied research trials is improvement of genetic selection strategies in an environment that replicates commercial production. This review provides context for evaluating top-cross progenies of sires selected based on either a standard index, emphasizing feed efficiency and carcass quality, or based on an experimental index, which emphasized feed intake, piglet vitality, and robustness.

Historic breeding goals

The swine industry is a vertically integrated industry that mainly uses large breeding companies to produce seedstock. Consistent improvement through genetic selection of elite lines by the breeding companies allows commercial producers an opportunity to increase the genetic merit of their breeding stock and thus increase profitability. This nucleus breeding system improves populations and gives the swine industry an opportunity to increase efficiency (Culbertson et al., 2017).

Genetic selection is a tool used across livestock industries to increase production efficiency and decrease costs for producers. In the swine industry, selection programs have typically emphasized traits with high economic value such as growth rate and decreased back fat thickness (Sonesson et al., 1998). More recently, consumer preference has driven the industry towards a leaner product with more emphasis on meat quality. These realities push breeding companies to produce efficient breeding stock with both greater quality and yield (Barbut et al., 2008). These performance traits are important in most swine production systems but in regions with high pig populations.

In the last 20 years, the goals of selection in the swine industry have emphasized increased leanness, feed efficiency, and growth rate (Barbut et al., 2008). The focus on feed efficiency is due to the fact that producers spend between 60 and 70% of their total cost of production on feed. Feed conversion ratio (FCR), a measure of feed efficiency, is the ratio of feed consumed per kg gained. Feed efficiency is strongly associated with feed costs and is a major influence on financial returns. Feed intake and weight gained are the two traits that compose FCR. To select for a superior FCR, a negative feed intake and positive weight gain are necessary for genetic gain. Thus, feed intake and weight

gain are clearly economically important traits (Patience et al., 2004). Another measurement of feed efficiency is residual feed intake (RFI), defined as the difference between observed feed intake and expected feed intake that is required for growth and maintenance. This approach incorporates body composition by using growth and maintenance requirements (Koch et al., 1963). Cai et al. (2008) found that after four generations of selection, RFI was a heritable trait (0.29) and pigs selected for low RFI had 1.36% greater feed efficiency ($P=0.09$) than unselected pigs. The work of Cai et al. (2008) demonstrated the efficacy of selection for feed efficiency.

The swine industry also uses genetic selection to improve growth rate. Two studies conducted by Pipestone Applied Research (unpublished data) in 2400 head commercial finishing barns compared growth performance of pigs sired by boars from two genetic lines: 1) a line selected for increased feed efficiency and 2) a line selected for reduced days on feed and leaner carcasses. Boars from each line were bred to females from a single dam line. Each genetic line was a commercially available sire line produced by a commercial breeding company. At marketing, pigs from line 2 were 1.0 kg heavier ($P<0.05$) and harvested after 3.6 fewer days on feed ($P<0.05$) than pigs sired by boars from line 1. Average daily gain (ADG) was 0.03 (live) and 0.02 (carcass) kg/d greater for pigs that had been sired by boars from line 2 on a live and carcass-basis, respectively ($P<0.05$). However, pigs that were sired by boars from line 1 had 1.8% greater feed conversion ratio. Pigs that were sired by boars from line 1 had a 0.25% greater average yield or dressing percentage while those sired by boars from line 2 had a 0.9% greater percentage lean and 2.2 mm greater loin depth ($P<0.05$). From this trial, it could be concluded that a commercial producer's preference for a line would depend on

the premiums offered by the producers harvest location, space or yardage cost, feed cost and if they are able to capture a premium on a leaner carcass. Line 1 would best fit a producer with a high feed cost, where line 2 would best fit a producer that needs a fast growing pig due to space limitations. Regardless, an understanding of regional limitations will help producers decide on the genetics that best fit their environment.

The second study was conducted six months after the completion of trial one. Trial two was conducted in the same facility, but the pigs were farrowed at a different sow farm. As in the first study, the same maternal line was used for both genetic groups. Boars used in the second study were from two commercially available genetic lines bred by two different companies. Line 1 was selected for feed efficiency and line 2 was selected for days on feed and carcass traits. The results of this study were similar to the previous study except: line 2 had a 4% more pigs receiving an optimum price at harvest and days on feed were similar for both lines. Line 1's feed conversion advantage was also repeatable on a live-basis but not when calculated on the basis of carcass weights. Mortality rates were approximately 3%; although acute disease affected some pigs, no major disease outbreaks caused severe mortality or morbidity (Holtkamp et al., 2013). Both of these studies were conducted in a facility that represented a high health, commercial US pig barn. Neither study had a known disease challenge.

In the previous two studies, maternal lines were the same when comparing different genetic groups. However, results by Johnson et al. (2002) suggest that maternal genetic effects can affect performance traits. Over an eight year period, maternal genetic effects of four breeds on post weaning performance traits were evaluated. Performance data was collected on purebred pigs in a commercial swine operation. Maternal breed

genetic effects were identified for 100 d weight, postweaning ADG, average daily feed intake (ADFI), loin eye area (LEA) and back fat depth (BF) for the pigs born to Landrace females. Pigs born to Yorkshire females also showed maternal breed genetic effects for 100 d weights, wean – finish ADG, LEA and BF ($P < .05$). Currently, most commercially available maternal lines are composed largely of Yorkshire and Landrace. This study shows variation in performance by maternal genetic group. From these results, one can conclude the importance of controlling for maternal genetic effects when assessing performance of piglets from multiple litters.

Genetic mitigation of disease challenges

Breeding goals for the swine industry emphasize economically important production traits like a lean and efficient carcass. Studies have been completed showing success of genetic selection on performance traits in the swine industry (Cai et al., 2008; Pipestone Applied Research, unpublished data). Still, the environment of a pig barn is rarely unaffected by various pathogens. More recently, researchers have been working to include phenotypes for resilience to increase overall genetic improvement of the swine industry (Merks et al., 2012).

Resilience while infected with a disease-causing pathogen may be crucial to agricultural systems. Resilience is generally defined as an individual's ability to cope with unpredictable perturbations. Globally, swine producers deal with increased cost arising from affliction with porcine reproductive and respiratory syndrome virus (PRRSV) (Neumann et al., 2005). The PRRSV greatly increases the rate of reproductive distress and respiratory illness in growing pigs.

The porcine reproductive and respiratory syndrome (PRRS) Host Genetics Consortium (PHGC) coordinates projects to explore the host genome following infection with PRRSV. The PHGC has investigated both the genotypes and phenotypes involved with the host response to PRRSV and estimated the heritability of those phenotypic traits that predict response to PRRSV infection (Hess, 2016; Boddicker et al., 2012; Boddicker et al., 2014). In fact, Hess (2016) estimated heritability when infected with NVSL, a virulent strain of PRRSV, results were moderately high for both viral load (VL) and weight gain (WG) (0.31 ± 0.06 and 0.33 ± 0.06), respectively. Additionally, the PHGC has developed experimental infection models that allow verification of phenotypes and

genotypes that predict PRRSV resilience (Lunney et al., 2011, Boddicker et al., 2012).

Research has shown that host response differs following infection with PRRSV in diverse genetic groups of pigs (Dunkelberger et al., 2015; Petry et al., 2005; Vincent et al., 2005).

Studies have been done to investigate resilience of swine to PRRSV (Greiner et al., 2000, Dunkelberger et al., 2015; Hess, 2016). Resilience is defined here as a pig's successful ability to maintain performance following exposure to a pathogen and is a function of tolerance and resistance. Tolerance is defined as a pig's ability to maintain performance given a specific pathogen load (Bishop et al., 2012). A pig's resistance is their ability to limit or completely prevent infection by the pathogen. A resilient animal can be tolerant, resistant or both when exposed to a pathogen. Many studies suggest both tolerance and resistance to PRRSV are moderately heritable (0.31 ± 0.06 and 0.33 ± 0.06) for WG and VL, respectively (Dunkelberger et al., 2015; Greiner et al., 2000; Hess, 2016, Petry et al., 2005).

Cost of PRRSV

Porcine respiratory and reproductive syndrome virus has caused a significant negative impact on the swine industry. It is considered the most economically devastating disease in the US swine industry and globally, it is considered one of the most economically important diseases to swine herds (Neumann et al., 2005). Each year PRRS costs US producers more than 77 million dollars, which include diagnostics, immunizations and treatments. Other outbreak related costs, such as implementing biosecurity efforts, may cost US producers up to 191 million dollars annually. In 2013, it was estimated that in total the PRRSV cost producers more than three dollars per head marketed (Holtkamp et al., 2013). This estimate includes preventative, costly measures

taken by producers to potentially reduce the disease or handle an outbreak (Holtkamp et al., 2013).

History of PRRS

In North America, PRRSV was first detected in the late 1980s (Lewis et al., 2007; Hill 1990). The disease resulting from infection with PRRSV was originally named “mystery swine disease” until 1991 when researchers in the Netherlands were the first to find the causative agent was a small, enveloped RNA virus (Wensvoort et al., 1992). At approximately the same time that the virus was discovered in North America, a virus causing pigs to show similar symptoms was discovered in Europe. The European strain of PRRSV (type 1) is genetically different from the North American strain (type 2). Originally, clinical signs displayed by infected pigs appeared similar and the two strains of virus shared approximately 60% of their nucleotide sequence (Kim et al., 2010). Veterinarians first noticed an increase in reproductive losses of late-term sows, and if born alive, piglets were weak and lethargic. In the growing phase, pigs were lethargic and had severe pneumonia, resulting in increased mortality and morbidity (Lunney et al., 2010). Prior to 2011, limited studies were completed comparing viral load and clinical signs between infections of PRRSV type 1 and type 2. Martinez-Lobo and colleagues (2011) experimentally infected six groups of pigs with PRRSV: three groups were infected with different isolates of type 1 and three groups were infected with different isolates of type 2. Using a mean area under the curve to quantify clinical scores weekly from 0-21 dpi, pigs infected by type 2 PRRSV presented with significantly longer and more severe clinical respiratory symptoms. No differences were observed between pigs infected with type 1 and 2 PRRSV for all other symptoms of disease, viral load and viral

distribution after infection. Thus, type 2 PRRSV caused increased severity of respiratory illness in pigs relative to the type 1 virus, which was independent of viral load or distribution.

Etiology of PRRS

The PRRSV is a small, single-stranded, enveloped, positive-sense RNA virus and belongs to the family Arteriviridae (Benfield et al., 1992). Its replication rate is fast and error-prone, leading to a high neutral mutation rate and a higher recombination rate with other strains of PRRSV (Brar et al., 2014). This high mutation rate provides the PRRSV with an evolutionary advantage allowing it to adapt quickly to changing environmental conditions. The virus increases rate of replication in cells of the blood monocyte and porcine alveolar macrophage (PAM) lineage by evading viral recognition mechanisms (Duan et al., 1997). These cells are actively involved in the innate immune response of the host (Lopez-Fuertes et al., 2000). It does so by altering activation of innate immune cells which decreases immune surveillance. Thus, PRRSV decreases the immune response of the lung. When the virus inhibits the innate activity of pulmonary macrophages, the host becomes susceptible to secondary pathogens (Gomez-Laguna et al., 2013).

PRRSV Isolate 174

PRRSV 174 is an isolate with restricted fragment length polymorphism pattern that emerged in the United States in 2014. It had evolved from the 184 family of PRRSV. At least 14 infections with PRRSV 174 have occurred in breeding herds that were previously vaccinated against the PRRSV (Geelen et al., 2018). The virulence of

the isolate played a major role in levels and length of viremia, humoral response, weight gain and mortality rates (Johnson et al., 2004). Pigs infected with non-PRRSV 174 isolates average 3-5% mortality, which may extend to approximately 30% in extreme cases (Nathues et al., 2017). In contrast, infection with PRRSV 174 has been associated with greater rates of mortality in finishing pigs; up to 50% mortality and morbidity has been observed (Perez et al., 2015). The PRRSV 174 isolate is a highly pathogenic, virulent strain of the virus that is prevalent in the US swine industry (Dee et al., 2018),

Clinical Disease

The PRRSV virus can infect pigs of all ages and production types. In breeding herds, PRRS may cause reproductive failures including late-term abortions, stillborn and mummified fetuses. Although the PRRSV causes reproductive failure its etiology not well understood. However, it is known that the virus causes the most severe reproductive failures when sows are infected in the final trimester of pregnancy (Zimmerman et al., 2006). In growing pigs, symptoms of PRRSV infection typically include decreased performance and an increase in the number of pigs that are afflicted with respiratory diseases such as pneumonia. Risk of secondary infections dramatically increases after infection with PRRSV, thus increasing the mortality rate (Rowland et al., 2012). The virus can persist in tissue for long periods of time. Zimmerman et al. (1992) was the first to show persistence of infection, by demonstrating transmission of PRRSV from an infected sow to her naïve piglets 99 dpi. The virus has still been found in experimentally infected weanling pigs up to 150 dpi (Allende et al., 2000).

Management of Disease

The cost of PRRS pushes veterinarians and producers to find more effective management tools. Vaccines to immunize pigs against PRRSV are commercially available for producers. However, the effectiveness of the vaccine depends on the similarity of the strain of PRRSV that is present in the production environment and the strain of PRRSV used to produce the vaccine. As stated earlier, genetic diversity of the PRRSV is high, and thus the virus that is present in the production environment is likely to be genetically different from that used in producing the vaccine (Kim et al., 2011). If the disease and vaccine strains are genetically homologous, vaccine protection can be effective. Unfortunately, Lager et al. (1999) has shown up to 20% genomic difference in strains of the same type. This variability within the PRRSV genome is thought to explain the inefficiencies of vaccines to cross-protect against all strains (Lunney et al., 2010). Antigenic and biological differences in isolates of the PRRSV have been reported (Meng, 2000). Differences in virulence have been observed among various isolates (Wensvoort et al., 1992). These studies show the difficulties of creating a targeted efficacious vaccine.

Nonetheless, PRRSV vaccines have been available to producers for over 25 years and are widely used to help combat the disease. A modified live vaccine (MLV) is the most common commercially used vaccine type. The MLV vaccines have protected against clinical diseases when animals are infected with a homologous strain (Geldhof et al., 2012). Still, safety concerns exist when using a modified live or live vaccine, including risk of reversion to virulence (Kimman et al., 2009).

Biosecurity is defined as the proactive protection of an animal herd from the introduction of any infectious agents. Biosecurity is a major tool used to prevent disease

and control the large amount of potential contaminants. Pathogen entry into a barn can occur through many different routes. One route is through genetic material that is regularly introduced into sow farms in the form of semen or replacement females (Amass and Clark, 1999). Additionally, contamination of feed and feed ingredients may be a vector of disease transmission (Dee et al., 2016). Employees, visitors, birds and rodents are additional vectors of disease transmission (Pitken et al., 2009). Following adequate down-time, or a minimum time spent away from pigs with an unknown health status prior to entry into other pig barns, shower and disinfectant protocols are crucial for biosecurity to be effective. Although biosecurity is important for preventing PRRSV introductions, it is not 100% effective (Toman et al., 2017). Elimination of PRRSV virus on a farm is possible and many elimination techniques are practiced. Herd closure is a technique that exposes the herd to either live virus or modified-live vaccine virus and closes the herd, where no new gilts are introduced. This method reduces virus spread over time because no new naïve animals are introduced. Once the farm stabilizes, naïve gilt introduction is possible (Gillespie and Carroll, 2003). Test and removal is another elimination technique that includes blood testing the entire herd and removing any positive animals. Dee et al. (2001) demonstrated this method to be successful for five chronically infected breeding herds of <1500 animals per herd. Dee (2004) successfully repeated this elimination methodology on 30 farms with larger populations and showed it to be efficacious. Still, this method has limitations: the labor required for removal of positive animals and cost of diagnostics. Unlike an effective biosecurity protocol, any elimination method does not prevent future infections.

Host Genetic Response to PRRSV

Many studies have identified genetic variation among pigs in host response following a PRRSV infection (Halbur et al., 2011; Lewis et al., 2007; Lewis et al., 2009, Lewis et al., 2009). Lewis et al., (2009) estimated genetic variation of the host response to tolerance of the PRRSV before and after a PRRS outbreak in commercial sows. The results showed within-breed genetic variation of commercially relevant traits after PRRS infection. Halbur et al., (2011) showed more severe lung scores in Hampshire pigs than Duroc or Meishan pigs following a PRRSV inoculation. Lewis et al. (2009) saw a similar result, where the pigs with Meishan genetics were more adversely affected by PRRSV than the European breeds studied.

Petry (2005) studied 400 non-vaccinated pigs, one-half of which were a Large White-Landrace line, selected for litter size over 20 generations, and one-half were a Hampshire-Duroc line, selected for lean growth and received from a commercial facility. Within each line, one-half of the pigs were challenged with PRRSV isolate 97-7985, the other half of each line was considered the control. Body temperature via rectal probe, blood collection to analyze viral load levels, and body weights were collected at inoculation (d 0), d 4, d 7, and d 14. All animals were euthanized and necropsied on d 14. Results showed a significant line effect post-inoculation and a significant interaction effect between line and treatment (challenged vs control) and day. This study provided early evidence of genetic variation in the mechanisms that induce immune response to the PRRSV.

Selection for Disease Resilience

Resilience to disease is the host's ability to maintain performance following exposure to a pathogen. A host with high resilience is able to limit the negative impacts that pathogens may have on the host and its performance. Unlike host resistance, which refers directly to the host's ability to prevent or limit infection, tolerance includes all immune mechanisms that are unrelated to the reduction of the pathogen. Tolerance refers to the slope of performance on pathogen load. Therefore, to quantify resistance or tolerance, pathogen load must be quantified. If pathogen load, resistance and tolerance are determined, a higher selection accuracy and more nuanced selection decisions may be possible (Bishop et al., 2012). Still, limitations like cost, labor, and data collection accuracy may indicate resilience is a much more practical as a selection criterion (Mulder & Rashidi, 2017). Following infection, a resilient animal can be tolerant, resistant or a combination of the two (Lough et al., 2016).

More recently, work has shown that genetic selection for resilience to PRRSV strains is possible (Rowland et al., 2012; Boddicker et al., 2014). Dunkelberger et al. (2015) measured growth and viral load of pigs following PRRSV infection in two groups of pigs selected for high (n=99) or low (n=97) residual feed intake (RFI). A lower residual feed intake represents a more feed efficient animal, whereas an animal selected for a higher residual feed intake has a greater actual feed intake than expected thus is less efficient. No growth differences in response to a PRRSV challenge were observed between animals selected for high and low residual feed intake, a 0.03 kg/d difference in ADG was detected ($P=0.10$). The more efficient (low RFI) group tended to have a lower viral load ($P=0.09$) and survival following PRRSV infection ($P=0.06$). These results

suggest that more efficient pigs are able to handle disease stress equally or potentially better than less efficient pigs.

The first genome-wide association study (GWAS) for host response to PRRSV was carried out by Boddicker et al. (2012). Data were from a previous study completed by the PHGC. A highly virulent isolate was used to infect healthy pigs one week after they were weaned. Weekly body weights were collected pre and post-infection to analyze weight gain (WG). Blood samples were collected biweekly to measure viremia pre and post-infection (viral load; VL). Both collections occurred through 42 dpi when all pigs were euthanized. Heritability estimates for both viral load and weight gain were moderate (30%). Supported by earlier studies (Hess, 2016; Boddicker et al., 2012; Boddicker et al., 2014), weight gain and viral load phenotypes were negatively correlated. The phenotypic correlations between VL and WG at 21 and 42 dpi were -0.22 ± 0.04 and -0.25 ± 0.04 , respectively. The genetic correlations of these two traits at 21 and 42 dpi were -0.54 ± 0.32 and -0.46 ± 0.35 , respectively. Boddicker et al. (2012) found that *Sus scrofa* chromosome 4 (SSC4) and *Sus scrofa* chromosome X explained a greater amount of variation in VL than any other region. SSC4 also explained some variation in WG.

Upon further analysis, one region on SSC4, a 33-SNP region, was responsible for a large proportion of the variation in the total genomic estimated breeding value (GEBV) of SSC4. Specifically, 6 SNP within the 33-SNP region accounted for 99.3% of the variance of the GEBV. One SNP, WUR1000125 (WUR), captured the greatest amount of genetic variation (99.4% VL, 99.3% WG42). Boddicker et al. (2012) showed that the WUR SNP had the largest effect of these six SNP on PRRSV VL. This region of the

genome is located near the guanylate binding protein 5 (GBP5), if fully functioning this protein helps in host defense, specifically, inflammasome assembly. If the host has a mutation at the GBP5 region and expresses the unfavorable allele, individuals are more susceptible to disease (Kommadath et al., 2017). The frequency of the favorable allele was 16.1% in Boddicker' et al., (2012), and the unfavorable allele has been consistently more frequent across studies (Dekkers et al., 2017; Boddicker et al., 2012; Boddicker et al., 2014). However, a low favorable allele frequency also suggests the selection for the favorable allele will be effective at increasing resiliency to PRRSV infections in commercial swine operations.

Greiner et al. (2000) also assessed the quantitative relationship of viremia and growth following PRRSV challenge. Pigs (n=96) were penned separately and challenged with a 2-mL dose of PRRSV isolate JA142. Similarly, body weight and blood were collected, but additionally feed intake was measured. All parameters were measured once pre-inoculation and then every 4 days until 24 dpi. A negative phenotypic correlation between viremia and growth was observed. A negative correlation was also observed between viremia and feed intake. For every log increase in serum PRRSV there was a 0.036 kg reduction in ADFI.

The concern over vaccine efficacy across strains has led researchers to assess host genetic response to genetically different isolates of PRRSV. Hess (2016) analyzed previous studies to compare host response to two different isolates and estimated genetic parameters of each isolate with WG and VL (Hess, 2016). This study analyzed 15 previous trials using either isolate NVSL-97-7895 (NVSL) or KS-2006-72109 (KS06). Correlations of WG and VL with the frequency of WUR genotypes were consistently

negative for both KS06 (-0.52 ± 0.17) and NVSL (-0.74 ± 0.10). This study supports previous research that the favorable allele is dominant and the genetic correlation of WG and VL are moderately negative. When infected with NVSL, Hess (2016) found that the WUR SNP was associated with reduction in viral load, potentially by controlling the rate of virus replication. This effect was observed in the WUR genotype's significant effect on peak viremia in both isolates. On the other hand, there was no significant association between WUR genotype and growth rate in pigs infected with KS06, the less virulent strain. A more virulent strain of PRRSV may be needed to observe a significant association between the selected SNP and weight gain (Hess, 2016).

Following a PRRS outbreak, it is rare that PRRS is the only disease in the barn. Many studies assess PRRS resilience in facilities that contain pigs that are free of other common disease and where PRRSV is the only detectable virus (Dunkelberger et al., 2015; Greiner et al., 2000; Petry et al., 2005). The most successful example of changing disease resilience through selection in swine is the response to F18 *E. coli* infection. *E. coli* F18 causes increased diarrhea in pigs which leads to significant mortality and morbidity. If pigs do not have the F18 receptor, this strain of *E. coli* is unable to colonize the porcine gut epithelium. Therefore, selection for pigs lacking the F18 receptor has proven successful for countries like Belgium that have a very high prevalence (96%) of F18 *E. coli* (Coddens et al., 2008).

Magnusson (1998) selected pigs for high and low combined cell-mediated and antibody immune responses were infected with *Mycoplasma hyorhinis*. The results of the study show selection has an effect on *Mycoplasma hyorhinis* susceptibility, although no clear advantage was shown by either group (Magnusson, 1998). Kadowaki (2012) has

shown that selection for resistance to swine *Mycoplasmal pneumonia* over five generations has responded to genetic selection and demonstrated the potential of selection for disease resistance.

More recently, Tibbs et al. (2018) completed a study assessing natural antibody (NAb) levels in healthy pigs exposed to natural challenges including PRRS disease, bacterial, and other viral infections. Results of this study showed a positive phenotypic correlation between IgG NAb and IgM NAb for all four antigens tested ($P < 0.001$). IgG NAb and IgM NAb levels were also both moderately heritable (0.11-0.19 and 0.27-0.39, respectively). These results show that genetic selection could be a useful tool to improve NAb levels. A review by Guy et al. (2012) stated the need for more studies that describe and account for environmental factors when assessing disease resistance and tolerance. To always assume a constant environmental effect in pig barns is unrealistic. The PRRS virus predisposes swine populations to bacterial and viral infections, with the likelihood of secondary infections occurring with increased virulence of the PRRS virus (Gomez-Laguna, 2013; Hess, 2016).

Conclusion

Genetic selection has been widely used in the swine industry to select for economically important traits such as feed efficiency and growth rate. This is important for swine producers because feed is the largest cost to producers in the growing phase and as pigs become more efficient, the amount of feed necessary to achieve an ideal market weight will decrease. Improved health and robustness to disease are also becoming increasingly important for modern pig production. Results from previous studies demonstrate the potential of using genetic selection to breed pigs for increased resilience to PRRSV-infection. Therefore, breeding pigs for improved resilience to PRRS may be used as an additional tool to reduce morbidity, mortality, and economic losses due to PRRSV-infection.

Results from previous studies also provide evidence of genetic variation in response of pigs to infection with pathogens commonly found in production settings, suggesting the potential of using genetic selection to breed pigs for improved general robustness to disease in commercial production. Due to increased susceptibility to polymicrobial diseases following PRRSV-infection, there is a need for more studies conducted in commercial-like facilities to allow secondary diseases to develop in the barn. Evaluating genetic resilience of pigs following PRRS and secondary disease will offer repeatable results to producers. Researchers need to use caution when conducting large-scale disease challenge models with virulent diseases. Potential concerns like excessive mortality and morbidity could affect the results and increase trial costs. A well-designed pilot study gives confidence in the experimental design and acceptability of potential outcomes.

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Chapter 2

PILOT STUDY

Introduction

Completion of a pilot study allows researchers to “try-out” methods or materials to give advanced warning on areas of potential failure in the main study (Van Teijlingen and Hundley, 2001). Leon et al., (2011) stated that pilot studies are a vital step in understanding the experimental design and potential protocol modifications for a larger, main study. When developing the protocol for chapter 3, the use of a robust isolate was crucial to illicit a strong disease response. The use of a local, relevant isolate was also important. PRRSV 174 is common in the Midwest and has been repeatedly shown to have a high degree of pathogenicity (Dee et al., 2018). Perez et al. (2015) found upwards of 50% mortality following a PRRSV 174 outbreak, where previous local isolates caused no more than 30% mortality in finishing pigs.

Commercially available PRRSV vaccines have been used in the swine industry for over 25 years and include modified-live and killed vaccines. Killed vaccines offer a stability of storage advantage. However, at this point, no protection or prevention of the disease has been shown after vaccination with a killed PRRSV vaccine (Scortti et al., 2006). Thus, producers prefer to use a modified-live PRRSV vaccine. PRRSV modified-live vaccines have shown to significantly reduce viremia and clinical signs following a PRRSV infection (Linhares et al., 2012).

The use of a virulent disease in a large-scale, experimental infection model could potentially cause an excessive mortality rate. Therefore, prior to conducting the main study, we estimated mortality in vaccinated and non-vaccinated pigs and tested whether PRRSV-1-7-4 is a suitable, and not excessive, isolate to experimentally infect 100% of the population. Therefore, the objectives of the pilot study were to answer two questions.

- 1) What are the clinical effects of PRRSV 174 challenge?
- 2) What is the effect of PRRSV vaccination on these outcomes?

Materials and Methods

Welfare Statement

Prior to the start of this study, Pipestone Applied Research (PAR) institutional animal care and use committees (PAR IACUC 1-18) reviewed and approved the trial protocol, mortality standards and caretaker handling certification. Throughout the trial these guidelines were upheld. A visual assessment of all pigs and the environment in which they lived, including verification of food and water source, was completed daily by a caretaker under the direction of the site veterinarian. The caretaker conducted the daily assessment using the individual pig care (IPC) scoring system (Pineiro et al., 2014) that classifies animal health status. The system classifies “A” as acute sickness, “B” as sub-acute sickness and “C” as severe, chronic illness. Pigs classified as a “B” or “C” were given antibiotic treatment if possible. If the approved protocol prevented antibiotic treatment, pigs classified as “B” or “C” were monitored more frequently. If deemed immobile and unable to eat or drink, the pig was euthanized. Pigs were humanely euthanized by a qualified caretaker that had been trained by the Pipestone Welfare Department and veterinarian.

Animal Source, Housing and Post-Weaning Experimental Design

Pigs (n=200) were placed into a nursery near Jackson, MN. All pigs were confirmed PRRSV wild-type negative. Just over 4 weeks prior to inoculation, pigs (n=100) were randomly allocated to the unvaccinated group (UnVAX) and shipped to the research nursery located near Edgerton, MN. All pigs that stayed at the original nursery near Jackson, MN received a 2 mL PRRSV modified-live virus vaccine (Ingelvac

PRRSV ATP, Boehringer Ingelheim) (VAX). On wean day, -2 days post-infection (dpi), the vaccinated pigs were shipped to the research facility. Upon arrival, pigs were placed into pens by vaccine status. Gender was balanced within each pen. Therefore even-numbered pens contained barrows and gilts of vaccinated pigs and odd-numbered pens contained barrows and gilts of unvaccinated pigs. Pen weights were taken once pen allocation was established.

PRRSV 174 Inoculation

At 0 dpi, all pigs were experimentally infected with $2 \times 10^{3.5}$ TCID₅₀ of PRRSV lineage 1 isolate 174. Homology between the virus and vaccine strain were 87%. Following guidelines from Dee et al. (2018) that used the same pathogenic variant of PRRSV, regular visits by the attending veterinarian at Pipestone Vet clinic were conducted to assess when antibiotic intervention was necessary. A “watch” list was created daily by the caretaker showing a list of unthrifty pigs that are sick and require intervention. When the watch list reached 20% of the population, mass medication would be administered. This occurred at 7 and 14 dpi. At 7 dpi, Excede (ceftiofur crystalline free acid, Zoetis, Parsippany, NJ) was administered due to the respiratory symptoms associated with the PRRS disease. At 14 dpi, Excede and Predef (anti-inflammatory, Zoetis, Parsippany, NJ) were administered, again to reduce the respiratory symptoms associated with the PRRS disease and Predef to reduce fevers shown in the pigs.

Phenotype Collection

At 7 and 14 dpi, all pigs were graded using the Galina robustness score (Pantoja et al., 2013). This system assigns each pig a value of 1-5 based on general disease clinical signs shown. A pig scored as a 1 is a normal healthy pig showing no signs of disease, a “2” pig shows early signs of disease, a “3” pig is showing moderate signs of disease, a “4” pig has advanced clinical disease signs and a “5” pig is a euthanasia candidate. Mortalities were recorded throughout the study. This trial was terminated four weeks after challenge.

Statistical Analysis

Data collected from 0 to 24 dpi were analyzed as a linear mixed model in R. For the mortality and robustness score data to be analyzed at the pen level, the outcome and robustness scores assigned to each pig were averaged within the pen and represented a % mortality, average robustness score (7 dpi.), average robustness score (14 dpi.) for each pen. The following model was used for all traits listed above:

$$y = Vaccine_i + e$$

In this equation, y represents the response variable (mortality or robustness score), $Vaccine_i$ represents the i^{th} vaccine status (VAX or UnVAX).

Results

The mortality rate for the vaccinated group was 5% (± 0.03) while the unvaccinated group had a 22% (± 0.03) death rate ($P < 0.01$). At 7 dpi, the vaccinated group averaged a 2.59 (± 0.13) on the robustness scale, while the unvaccinated group averaged a 3.13 (± 0.13) on the robustness scale ($P = 0.01$). At 14 dpi, the vaccinated group averaged a 2.04 (± 0.15) on the robustness scale, while the unvaccinated group averaged a 3.25 (± 0.15) on the robustness scale ($P < 0.01$) (Table 2.1).

Discussion

Conducting a pilot study allows researchers the opportunity to understand potential issues with an established protocol and the experimental design involved. An experimental infection model with PRRSV 174 could potentially cause a significant mortality and morbidity in a large commercial finisher. Therefore, the objectives of the pilot study were to understand the clinical effects PRRSV 174 challenge in vaccinated and unvaccinated pigs.

Results of this study showed the effectiveness of a modified-live PRRSV vaccine against an experimental infection with PRRSV 174. Expanding the mortality rates seen in the pilot study to the scope of the study in Chapter 3 would be expected to result in an excessive mortality rate of over 320 pigs. Additionally, the unvaccinated group had a greater average Galina score at both 7 and 14 dpi. Suggesting that morbidity was also greater in the unvaccinated group.

A major extrinsic effect on performance that can increase pig weight variation within a barn is exposure to pathogens. Thus, no surprise that variation in the robustness score was greater at both 7 and 14 dpi in the UnVAX group. This variation in morbidity translates to greater weight and performance variation within the UnVAX group.

Previous work done by Patience (2004) emphasizes the importance of decreased pig size variation across a swine barn. During the growing phase, dietary nutrients are less efficiently utilized when pig size within a pen is high (O'Quinn et al., 2001). Increased variability in finishing barns decreases the on-farm efficiency. Therefore, the pilot study suggested that the use of a vaccine can decrease variation across a group of pigs if faced with a PRRS disease outbreak.

Conclusion

Based on the results, a PRRSV modified-live vaccine will be administered to all pigs four weeks prior to experimental infection with PRRSV 174. We concluded that vaccination was necessary to keep mortality rates manageable. Still, a 5% mortality rate in the vaccinated pigs suggest the use of PRRSV 174 in the pilot study provided a robust challenge to the pigs regardless of vaccination status.

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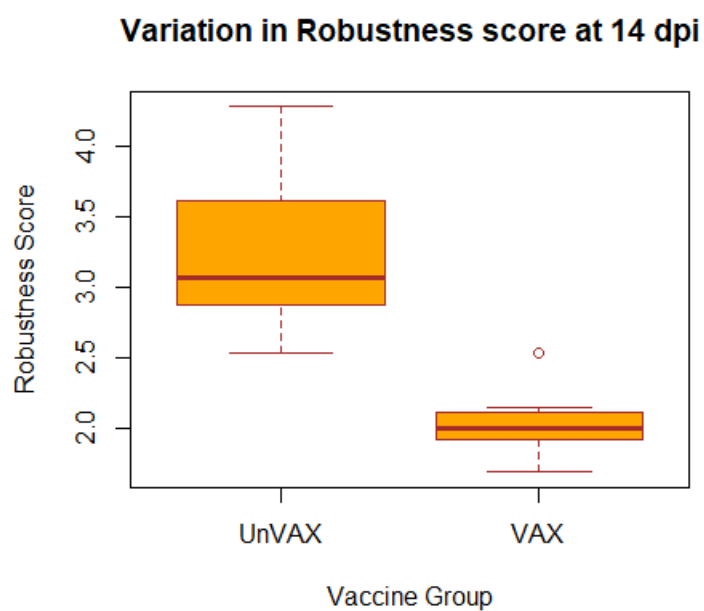
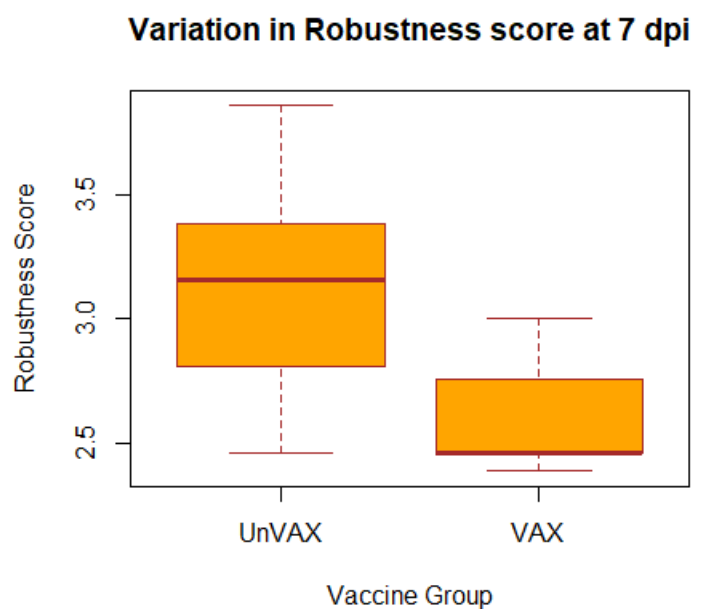
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Table 2.1: Comparison of percent mortality and robustness scores between (VAX) vaccinated pigs and (UnVAX) unvaccinated pigs. (SEM)

| Sire Group | | | |
|----------------------------------|-------------|--------------|---------|
| | VAX | UnVAX | P-value |
| Mortality (%) | 5.0% (0.03) | 22.4% (0.03) | <0.01 |
| Average Robustness Score, 7 dpi | 2.59 (0.13) | 3.13 (0.13) | 0.01 |
| Average Robustness Score, 14 dpi | 2.04 (0.15) | 3.25 (0.15) | <0.01 |

Figure 2.1: Variation in Robustness Score at 7 and 14 dpi.



Chapter 3

PERFORMANCE DIFFERENCES BETWEEN TWO GROUPS OF COMMERCIAL
PIGS FOLLOWING EXPERIMENTAL INFECTION WITH PRRS VIRUS 1-7-4

Introduction

The swine industry has long used genetic selection to increase production efficiency by selecting for economically important traits (Sonesson et al., 1998). More recently, producers have realized the importance of resilient production animals which can decrease costs and increase welfare and sustainability. Consequently, breeding objectives should shift to include selection for increased resilience, which is the ability to maintain performance following exposure to a pathogen (Greiner et al., 2000).

Porcine reproductive and respiratory syndrome (PRRS) virus is one of the most economically devastating viruses to global pork producers (Neumann et al., 2005). Due to the nature of the virus, a decrease in immune surveillance occurs allowing secondary pathogens to cause disease in affected animals (Gomez-Laguna et al., 2013). In 2013, it was estimated that the disease and associated preventative measures cost producers up to three dollars a pig marketed (Holtkamp et al., 2013). Other tools such as vaccination and biosecurity are available to the industry but neither offer full protection from the virus. Lack of full protection is largely due to a fast, error-prone replication rate of the PRRSV that allows it to mutate quickly (Brar et al., 2014). Still, PRRSV vaccines are used by producers with success dependent on the genetic similarity of the strain of virus used in producing the vaccine and the strain of virus that is present in the production environment (Lager et al., 1999; Lunney et al., 2010).

The objective of this study was to evaluate performance differences in pigs sired by boars that had been selected from a single population using either a standard or experimental selection index following experimental infection with PRRS virus 1-7-4. The standard index emphasized feed efficiency and carcass quality. The experimental

index emphasized feed intake, piglet vitality and robustness. Isolate 1-7-4 is a prevalent strain within the Midwest that is considered highly pathogenic and virulent (Dee et al., 2018; Geelen et al., 2018; Perez et al., 2015).

Materials and Methods

Welfare Statement

Prior to the start of this study, the South Dakota State University (SDSU) and Pipestone Applied Research (PAR) institutional animal care and use committees (SDSU IACUC 18-030A and PAR IACUC 1-18) reviewed and approved the trial protocol, mortality standards and caretaker handling certification. Throughout the trial these guidelines were upheld. A visual assessment of all pigs and the environment in which they lived, including verification of food and water source, was completed daily by a caretaker under the direction of the site veterinarian. The caretaker conducted the daily assessment using the individual pig care (IPC) scoring system (Pineiro et al., 2014) that classifies animal health status. The system classifies “A” as acute sickness, “B” as sub-acute sickness and “C” as severe, chronic illness. Pigs classified as a “B” or “C” were given antibiotic treatment if possible. If the approved protocol prevented antibiotic treatment, pigs classified as “B” or “C” were monitored more frequently. If deemed immobile and unable to eat or drink, the pig was euthanized. Pigs were humanely euthanized by a qualified caretaker that had been trained by the Pipestone Welfare Department and veterinarian.

Animal source and pre-weaning protocol

All pigs were sourced from a 5,000-head, PRRSV naïve, sow breeding farm located in northeastern South Dakota, USA. Topigs Norsvin parent females (Landrace x Large White) were mated using semen from a Topigs Norsvin synthetic sire line to produce the pigs used for this study. Sires used for this study were selected based on a

standard index (TN-S) and an experimental index (TN-E) for robustness to disease challenge. To select the sires for each group, a TN-S and TN-E customized index value was calculated for each boar from the stud used to supply the semen for the trial. The eleven boars with the highest TN-S customized index values and the eleven boars with the highest TN-E customized index values were selected as sires for the TN-S and TN-E groups, respectively. Customized indices were constructed using combinations of selected traits derived from the Topigs Norsvin Selection Index. The TN-S index included traits related to feed efficiency and carcass quality. The TN-E index included traits related to robustness and feed intake. When the immune system is under stress due to disease challenge, a decrease in feed intake leading to anorexia can occur (Li & Patience, 2017). Thus, increased feed intake was predicted to improve resilience to a disease challenge.

Using artificial insemination and gestation stall housing, an equal number of sows and gilts were randomly bred to boars from one of the two sire groups. Unusual for the commercial industry, single-sire semen was used. Therefore, if a sow or gilt showed signs of heat on day 2, she was bred again with the same boar number as day 1. If needed, she was bred again on day 3, again with the same boar number. Sows were farrowed in crates. Once farrowing occurred, all piglets were tagged with a Caisley ear tag (Caisley Eartag Limited, North Yorkshire UK). This ear tag simultaneously took a tissue sample from the piglet when the tag was inserted into the ear. The ear tag identified sire group for each piglet. Information including birth weight, dam ID and parity were recorded at birth. Additionally, a tissue sample was taken from the ear of each dam. About 1,000 pigs of each sire group were tagged. Eleven unique boars from

each sire group were bred to 69 (TN-E) and 72 (TN-S) dams. The breeding farm staff followed their standard operating procedures through weaning, including “fostering” of piglets. Fostering piglets allowed staff to move newborn piglets, within 24 hours of birth, of extreme size (small or large) relative to their littermates to another dam, matching litter size to sow teat count and limiting competition amongst littermates. The piglets’ biological and foster dams were recorded. At approximately 21 days of age, piglets were weaned to the finishing site if they weighed >3.6 kg and did not show clinical illness, lameness or deformity. Piglets that were unable to be weaned due to these classifications were humanely euthanized. Per sow farm protocol, all pigs meeting the trial criteria were given .5 cc of Baytril (Bayer Healthcare LLC) prior to weaning.

Housing and post-weaning experimental design

The pigs weaned to a 2400 head wean-to-finish barn located in southwestern Minnesota, USA. This barn is tunnel ventilated with 2 rooms consisting of 39 and 42 pens, although only 54 pens (26 and 28 per room) were used for this study. Each room contains a separate, but identical, ventilation system (Expert Series, Automated Production) that regulates barn environment by using a temperature curve. Individual and pen wean weights were taken and a Radio Frequency Identification (RFID) tag was placed opposite the Caisley tag in each pig’s ear. Weaning weights for TN-E and TN-S sired pigs averaged $6.15 (\pm 0.13)$ and $6.20 (0 \pm .13)$ kg, respectively. Across the barn, the wean age ranged from 14-29 days of age and the average wean age was $20.3 (\pm 0.3)$ and $20.4 (\pm 0.3)$ d for TN-E and TN-S sired piglets, respectively. Due to the large number of pigs entering the research barn, the pigs were received over 5 weaning events. Thus, wean weight, wean weight date and wean age varied within treatment group but was not

significantly different across treatment groups. On the final wean day, all pigs were vaccinated with a 2 mL PRRSV modified-live virus (Ingelvac PRRSV ATP, Boehringer Ingelheim).

Because pigs were penned together by sire group, the experimental unit was the pen. The trial utilized a randomized block design with 27 blocks. Each block consisted of two pens, one containing pigs sired by boars from the TN-E line and one pen containing pigs sired by boars from the TN-S line. Pens within each block were located immediately adjacent to each other. Block was used to account for environmental variation such as humidity, temperature, air quality and other environmental factors across the tunnel ventilated barn. Each pen consisted of 27 pigs, which were randomly selected from the wean group, except that the smallest 27 pigs of each group were placed into a single block, limiting competition equally for the two small pens. This prevents fallout from the smallest group of piglets within their genetic group. Male and female pigs were penned together with an equal sex-ratio in each pen of a block. A 136 kg Crystal Spring 4-hole dry feeder was located in each pen, allowing 0.65 sq. m of floor space per pig and 34.93 cm head space per feeder hole. Additionally, each pen had 2 cup water dishes. Feed and water were provided *ad libitum*. An automated feeding system was used for all pens, which tracked the time feed was delivered and the amount of feed delivered to each pen (Feedlogic Corporation, Willmar, MN).

PRRSV 174 Challenge

Four weeks post-vaccination, pigs were challenged with PRRSV lineage 1 strain 174 injected intramuscularly (dose = $2 \times 10^{3.5}$ tissue culture infectious (TCID₅₀) dose) under the direction of veterinarians. Following guidelines from a previous study that

used the same pathogenic variant of PRRSV (Dee et al., 2018), weekly visits by both the attending veterinarian and the welfare director at Pipestone Vet clinic were conducted to assess when antibiotic intervention was necessary. A “watch” list was created daily by the caretaker showing a list of “B” or “C” pigs, using the IPC scoring system. When the watch list reached 20% of the population, mass medication would be administered. This occurred at 21 dpi, therefore, the entire barn received an IM injection of Excede (ceftiofur crystalline free acid, Zoetis, Parsippany, NJ) and Predef (anti-inflammatory, Zoetis, Parsippany, NJ). Excede is used to reduce the respiratory symptoms associated with the PRRS disease and Predef is an antinflammatory that reduces fever in pigs. At 26 dpi, water-soluble LinxMed (Lincomycin Hydrochloride Powder, Bimeda, Oakbrook Terrace, IL) was distributed through the water to all pens for 7 days. Lincomycin was used to combat pneumonia and arthritis symptoms in the pigs.

Diagnostic Testing

Starting the week prior to inoculation, weekly oral samples were taken via saliva rope collection. These samples were sent to South Dakota State University and tested for PRRSV and Influenza (IAV). If the sample came back positive for PRRSV prior to challenge, the virus was sequenced to confirm the vaccine strain caused the positive test result. Only the vaccine strain was found in the pigs prior to PRRSV inoculation. On a regular basis, mortalities were necropsied by a trained caretaker and samples were submitted to SDSU to monitor pathogens present throughout the study.

Phenotype Collection

Average daily gain (ADG), feed conversion ratio (FCR) and average daily feed intake (ADFI) were recorded and calculated for each treatment group at weaning and on 0, 13, 42, and 110 dpi. Marketing started on 111 dpi and pigs were marketed over a 5-week period on a fixed weight basis with a goal of 127 kg. All pigs that were sent to the packing plant weighing >104 kg void of defects including umbilical hernias and intact males were classified as full value (FV). Pigs weighing <104 kg or with a defect were sent to secondary markets and classified as light or defect cull, respectively. Pigs that died after weaning were assigned to a separate category. The FV pigs were harvested at a packing plant where hot carcass weight, % lean, back fat and loin depth was measured and recorded. Individual weights were collected on the morning of marketing and a hot carcass weight was collected during harvesting which were both used to calculate a carcass yield.

Statistical Analysis

Data collected during the weaning-to-finish period and 0 – 42 dpi were analyzed using a linear mixed model in R. For the final outcome (FV, light, defect, and mortality) and carcass data to be analyzed at the pen level, the outcomes assigned to each pig and carcass phenotypes were averaged within the pen and represented a % full value, % mortality, % defect cull, % light cull, % yield, % lean, back fat thickness, loin depth and hot carcass weight for each pen. The following model was used for all traits listed above:

$$y = Sire_i + Block_j + e$$

In this equation, y represents the response variable (final outcome or carcass traits), $Sire_i$ represents the i^{th} sire group (TN-E or TN-S) and $Block_j$ ($n=27$) represents

the j^{th} random location in the barn. Day 0 weight had a significant association with 0-42 ADG and FCR, and thus was used as a covariate in the statistical model for 0-42 ADG and FCR.

Another linear mixed model was used to estimate effect of sire group on birth weight and ADG from birth to weaning. The data were analyzed using the model:

$$y = Sire_i + Gender_j + Birthsow_{k(Sire)} + e$$

In this equation, y represents the response variable (birth weight or birth- wean ADG) of the individual pigs, $Sire_i$ represents the i^{th} sire group, $Gender_j$ represents the j^{th} gender of the pig and the random effect of birth sow represents the dam of each piglet and is nested within Sire. Effects of birth date and sire group by gender interaction were not statistically significant for either trait ($P > 0.10$) and thus were not included in the final model. A p-value of ≤ 0.05 was used as the criterion for statistical significance.

Results

Pre-wean outcomes

Table 3.1 shows the birth-to-weaning performance of the two genetic groups. The TN-S sired group was .07 kg heavier at birth ($P = 0.06$). Birth to wean ADG was not statistically different between groups. Males were 0.05 kg heavier at birth (<0.01). At weaning, the weaning weights ($P = 0.65$) and weaning ages ($P = 0.86$) were not different between sire groups.

Post-wean outcomes

There were no significant differences in ADG or ADFI during the wean-to-finish period ($P = 0.27$). During the period from weaning to harvest, the TN-S sired group had a 0.06 lower FCR ($P < 0.01$) than the TN-E sired group. Narrowing in on the challenge and post-challenge period, there was still no statistically significant difference in ADG between the sire groups. However, from 0 – 42 dpi, the TN-E sired pigs consumed 0.6 kg/d more than the TN-S sired group ($P < 0.01$). Again, the TN-S sired pigs had a lower FCR ($P < 0.01$) (Table 3.2).

Carcass Attributes

In regards to carcass attributes (Table 3.3), there were no statistically significant differences between sire groups for hot carcass weight, percent yield, back fat, or loin depth. The TN-S-sired pigs had a significantly greater % lean ($P = 0.02$).

Final outcomes

A greater number of mortalities were observed in the TN-E sired pigs (118 mortalities) than the TN-S sired pigs (105 mortalities), although this difference was not statistically significant (Table 3.4).

Pathogens detected

Pathogens detected throughout the study are shown in Table 3.5. The source farm was positive for influenza throughout this study. Therefore, the piglets were positive for influenza when they arrived at the research barn. Prior to challenge, most necropsied pigs were also positive for *Streptococcus suis*. Fecal samples collected from a subset of pens were positive for rotavirus, but that disease was limited to only a small number of pens and was cleared up prior to challenge. PRRSV 1-7-4 was detected in the pooled oral samples three days after challenge. Mortalities were necropsied and were positive for *Streptococcus suis*, *Actinobacillus suis*, *Haemophilus parasuis* and *Pasturella multocida*. In addition, at around eight weeks post-challenge, *Bronchopneumonia* and *Escherichia coli haemolytic* were detected in the tissue of necropsied pigs.

Discussion

Selective breeding is a tool used in many livestock species to increase the rate of genetic improvement (Nicholas, 1997). Feed costs amount to the greatest expense for swine producers, thus selection for improved feed efficiency and growth rate fit consumer and producer preferences (Barbut et al., 2008). More recently, producers realize the benefits of increased robustness in their pig populations. For these reasons, breeding objectives should be modified to breed pigs for improved health and survivability (Merks et al., 2011).

Globally, the PRRS virus has had a significant impact on swine producers. Since recognition of the virus in the late 1980s producers have faced major economic losses due to PRRSV. The severity and loss associated with the disease varies. Following infection with PRRS virus, the susceptibility of the host to secondary infection increases (Niederwerder et al., 2015). Due to evasion mechanisms of the virus, immune surveillance is less effective and polymicrobial infections are more likely to occur (Gomez-Laguna et al., 2013). Therefore, the purpose of this study was to assess performance differences in pigs sired by boars selected based on a standard (TN-S) or experimental index emphasizing resilience (TN-E) in a commercial facility following experimental infection with PRRS virus 1-7-4.

Performance characteristics between the TN-E and TN-S lines were not substantially different. Boars were selected using two different customized selection indices, but originated from the same population. Thus, only one-half generation of selection had occurred, which may be the main reason that minimal performance differences were observed between lines. In contrast, results from previous studies show

that significant performance and robustness differences existed between lines that were divergently selected over five to twenty generations (Dunkelberger et al., 2015; Doeschl-Wilson et al., 2009; Mpetile, 2014; Faure et al., 2013). Thus, selection based on each index over additional generations may result in greater performance differences between pigs sired by boars from each line. Dams of all of the pigs that were evaluated were of the same genetic line and multiplier to reduce the potential of sire x dam confounding effects.

Still, results of this study showed a significantly better FCR for the TN-S group during the wean-to-finish period and 0 – 42 dpi. Although the TN-E group had a significantly greater feed intake 0 – 42 dpi, ADG was similar for the two genetic groups. The TN-E sired boars were selected for increased feed intake, while the TN-S sired boars were selected for feed efficiency, so this result was not surprising. This result suggests that increased feed intake does not always lead to faster growth rates. Although not statistically significant, a 2% (± 0.02) greater mortality rate was observed for pigs sired by TN-E boars. Dunkelberger et al. (2015) showed that more feed efficient pigs may respond better to PRRSV infection. Because only the TN-S index emphasized feed efficiency, the present results were consistent with Dunkelberger et al. (2015). In addition, lean percentage was significantly superior for TN-S, the group sired by boars selected for feed efficiency. Many studies have reported selection for residual feed intake, a measure of feed efficiency, had carcasses with significantly greater percent lean (Smith et al., 2011; Arthur et al., 2009; Faure et al., 2013).

A robust animal is one which is capable of adapting to stressors while staying healthy and performing well (Herrero-Medrano et al., 2015). Regardless of health status,

mortality is still one of the largest causes of economic loss in swine production (Maes et al., 2001). Neumann et al., (2005) found that 88% of the total cost of PRRSV infections is attributed to decreased performance and increased mortality rates. The rate of FV pigs at harvest time is one of the most important measurements of robustness. The FV pigs represent a percentage of the population excluding mortalities, light and defect culls. These pigs were robust enough to tolerate the disease challenge and grow efficiently enough to be harvested above a minimum weight set by packing plants (104 kg). No significant differences in FV pigs were detected between the two genetic groups. The experimental group was selected for piglet vitality and robustness; potentially these phenotypes do not correlate with mortality. Each genetic group contained 27 replicates; to achieve 80% power at a significance level of 5%, a 30% difference would need to be observed. Cornelison et al. (2018) found only an 18% range in FV pigs of low and high natural disease challenge placed in the same environment. Detecting a 30% difference in FV between two groups infected with the same disease and raised in a common environment is unreasonable.

The increased rate of polymicrobial diseases following a PRRS disease outbreak suggests the importance of increased general disease immunity (Lunney et al., 2011). Therefore, conducting this study in a facility that is representative of commercial production is a strength of this trial. It also allows for more direct inference to commercial production. The rate of FV pigs marketed ranged from 81.8% (TN-E) to 83.7% (TN-S) between genetic groups. Cornelison et al. (2018) evaluated three levels of naturally occurring health challenges in three commercial barns having similar environments. The three levels of health challenges included low, moderate and high

exposure to pathogens. This resulted in 89.2%, 80.5% and 70.6% of FV pigs marketed, respectively. The moderate to high health challenged groups reflect the performance of the pigs in this study.

Surveillance of pathogens throughout this study represent a realistic array of diseases that would typically infect a pig barn affected by PRRSV. Yu (2012) reported that highly pathogenic PRRS virus accelerates the rate of infection and load of *Haemophilus parasuis*. Our results were consistent with Yu (2012); we detected, not only *Haemophilus parasuis*, but also Influenza, *Actinobacillus suis*, *Pasturella multocida*, *Bronchopneumonia* and *Escherichia coli haemolytic*. Assessment of wean to finish performance objectives in response to an experimental PRRS virus 174 infection with secondary infections had yet to be studied prior to this study being completed.

Rowland and colleagues (2012) identified that lack of control of observational data as a major limitation of field studies. Because we cannot control for environmental variables in field studies, including pathogen exposure, a larger number of animals are required to achieve sufficient power to identify differences among groups. Our study controlled PRRS virus exposure levels, used one maternal genetic line and balanced for parity, wean age and barn effect across both genetic groups. Cho et al., (2005; 2006) repeatedly found greater viral load concentrations of PRRS virus in younger pigs, suggesting the importance of balancing age at challenge between genetic groups. Block accounted for a large portion of variation in all statistical tests. This result is to be expected due to the large variation in temperature, air quality, humidity, and other environmental factors across a tunnel ventilated barn. The design of this study exercised much control over unknown variation while still assessing the pigs in a representative

commercial facility infected with a relevant, virulent strain and common secondary pathogens.

Conclusion

Between the genetic groups evaluated in this study, minimal differences in performance were observed. It is possible that genetic difference between the boar lines used in this experiment were not large enough to result in statistically significant differences between progeny sired by boars selected using the TN-S vs. TN-E indices. Another possibility for the lack of significant differences between sire lines is that the TN-E index is not effective at improving resilience and mortality rates of pigs in the face of a PRRSV challenge. Selection for multiple generations using each index may allow us to test which of the above explanations for our results is most likely. However, the TN-S pigs (selected for increased feed efficiency) were significantly more efficient throughout the entire study. These pigs also had a numerically lower mortality rate, suggesting the importance of feed efficiency rather than feed intake as an indicator for tolerance during a virulent disease challenge.

The scope of this study allowed collection of phenotypic and genetic data on over 1,400 animals after exposure to PRRSV. Additionally, further evaluation of genetic variation following PRRSV viral infection is possible. The data collected are a resource for future analyses to improve genetic selection of resilience to disease challenge.

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Table 3.1: Performance of pigs sired by Topigs Norsvin-Standard (TN-S) and -Efficiency (TN-E) boar groups from birth to weaning. (SEM)

| Sire Group | | | |
|------------------|-------------|-------------|---------|
| | TN-E | TN-S | P-value |
| Pigs, n | 727 | 730 | |
| Birth weight, kg | 1.45 (0.36) | 1.52 (0.30) | 0.06 |
| Birth - wean ADG | 0.22 (0.01) | 0.22 (0.01) | 0.95 |

Table 3.2: Performance of pigs sired by Topigs Norsvin-Standard (TN-S) and -Efficiency (TN-E) boar groups from wean to finish. (SEM)

| Sire Group | | | |
|-----------------------------------|---------------|---------------|---------|
| | TN-E | TN-S | P-value |
| Pens, n | 27 | 27 | |
| Wean Weight, kg | 6.15 (0.13) | 6.20 (0.13) | 0.65 |
| Wean Age, days | 20.33 (0.3) | 20.38 (0.3) | 0.86 |
| Wean to Finish | | | |
| Average market weight, kg | 124.37 (0.43) | 124.72 (0.43) | 0.33 |
| Average daily gain, kg/day | 0.76 (0.01) | 0.77 (0.01) | 0.27 |
| Average daily feed intake, kg/day | 1.87 (0.02) | 1.84 (0.02) | 0.11 |
| Feed conversion | 2.45 (0.01) | 2.39 (0.01) | <0.0001 |
| 0 – 42 dpi | | | |
| Average daily gain, kg/day | 0.56 (0.01) | 0.56 (0.01) | 0.82 |
| Average daily feed intake, kg/day | 1.22 (0.03) | 1.16 (0.03) | 0.01 |
| Feed conversion | 2.20 (0.02) | 2.08 (0.02) | 0.01 |

Table 3.3: Comparison of percent final outcomes between pigs sired by Topigs Norsvin-Standard (TN-S) and -Efficiency (TN-E) boar groups. (SEM)

| Sire Group | | | |
|------------------------------|--------------|--------------|---------|
| ¹ Final Outcome | TN-E | TN-S | P-value |
| ² Full Value, % | 81.8% (0.02) | 83.7% (0.02) | 0.39 |
| ³ Mortality, % | 16.2% (0.02) | 14.4% (0.02) | 0.29 |
| ⁴ Defect culls, % | 0.7% (0.01) | 0.5% (0.01) | 0.73 |
| ⁵ Light culls, % | 1.2% (0.01) | 1.4% (0.01) | 0.79 |

¹ Final Outcome is a binary outcome assigned to every pig at the end of the study.

² Full Value (FV) is assigned to pigs harvested at an optimum price to the packer, free of defects and >104 kg.

³ Mortality is assigned to pigs that die during the wean to harvest period.

⁴ Defect cull is assigned to pigs that were sold to a secondary market due to a genetic defect.

⁵ Light cull is assigned to pigs that were sold to a secondary market weighing <104 kg.

Table 3.4: Carcass performance differences between pigs sired by Topigs Norsvin-Standard (TN-S) and -Efficiency (TN-E) boar lines. (SEM)

| Sire Group | | | |
|--------------------------|--------------|--------------|----------------|
| Carcass Attribute | TN-E | TN-S | P-value |
| Hot carcass weight, kg | 92.60 (0.36) | 92.80 (0.36) | 0.68 |
| Yield, % | 74.4% (0.01) | 74.2% (0.01) | 0.17 |
| Back fat, mm | 17.5 (1.9) | 17.1 (1.9) | 0.13 |
| Loin depth, mm | 63.2 (4.8) | 63.7 (4.8) | 0.39 |
| Lean, % | 55.1% (0.2) | 55.7% (0.2) | 0.02 |

Table 3.5: Pathogens detected pre-challenge and post-challenge.

| Pre-Challenge | Post-Challenge |
|--|---|
| ² Influenza | ³ <i>Salmonella</i> |
| ¹ <i>Streptococcus suis</i> | ² ¹ PRRSv 174 |
| ³ Rotavirus | ¹ <i>Actinobacillus suis</i> |
| ³ <i>Salmonella</i> | ¹ <i>Haemophilus parasuis</i> |
| | ¹ <i>Pasturella multocida</i> |
| | ¹ Bronchopneumonia |
| | ¹ <i>Escherichia coli haemolytic</i> |

¹Detected in tissue samples

²Detected in oral samples

³Detected in fecal samples